



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61L 15/28	A1	(11) International Publication Number: WO 00/01425 (43) International Publication Date: 13 January 2000 (13.01.00)
(21) International Application Number: PCT/GB99/02093 (22) International Filing Date: 1 July 1999 (01.07.99) (30) Priority Data: 9814273.0 1 July 1998 (01.07.98) GB 9824667.1 10 November 1998 (10.11.98) GB (71) Applicant (for all designated States except US): AKZO NOBEL UK LIMITED [GB/GB]; Oriel House, 16 Connaught Place, P.O. Box 20980, London W2 2ZB (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): PATEL, Champa [GB/GB]; 13 Culworth Court, Foleshill Road, Coventry CV6 5JY (GB). BRAY, Roger [GB/GB]; 6 Hollinwell Close, Whitestone, Nuneaton, Warwickshire CV11 6TU (GB). (74) Agent: HALE, Stephen, Geoffrey; J.Y. & G.W. Johnson, Kingsbourne House, 229-231 High Holborn, London WC1V 7DP (GB).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: WOUND DRESSINGS AND MATERIALS SUITABLE FOR USE THEREIN		
(57) Abstract <p>Carboxymethylated cellulosic articles having degree of substitution in the range from 0.12 to 0.35 and in which the carboxymethyl groups are believed to be predominantly within the amorphous regions to the exclusion of the crystalline regions have usefully non-adherent properties as wound dressings. Such wound dressings may be made by carboxymethylating a cellulose fabric so that its absorbency is little greater after carboxymethylation than beforehand and the degree of substitution is as stated above. Carboxymethylation can be carried out by contacting cellulose II fibres or other articles with a solution containing sodium hydroxide, sodium chloroacetate, water and ethanol. The solution may contain from 4 to 8 percent by weight sodium hydroxide and from 50 to 60 percent by weight water (including water in the fibre) or the weight ratio of sodium hydroxide to water (including water in the article) may be from 0.095 to 0.115 and the weight ratio of cellulose in the article to water (including water in the article) may be from 0.22 to 0.28.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

WOUND DRESSINGS AND MATERIALS SUITABLE FOR USE THEREIN

Field of the invention

This invention relates to wound dressings, in particular to dressings in fabric form and other forms suitable as contact layers for exuding wounds, and to methods for the manufacture of such dressings and of materials for use therein.

Commonly-used wound dressings include foams, sponges and fibre-based materials such as gauzes and waddings, for example of cotton or viscose rayon. Such fibre-based materials tend to adhere to the wound surface and are accordingly difficult to remove, after use, in one piece and without causing trauma to the patient. Known wound dressings also include advanced dressings based for example on alginates or on various kinds of hydrocolloids or hydrogels, but such dressings are relatively expensive and are accordingly used in general only when clinical needs so recommend. There exists a desire for wound dressings which possess at least some degree of absorbency, but which are sufficiently non-adherent that they are capable of being removed from a wound in a single piece without shedding fibre fragments and without trauma to the patient, and which are inexpensive in comparison with advanced dressings.

25 Background art

WO-A-94/16746 discloses a wound dressing in which the wound-contacting surface comprises carboxymethylcellulose (CMC) filaments capable of absorbing at least 15 times, preferably at least 25 times, their own weight of 0.9% by weight aqueous saline solution (as measured by a defined free-swell absorbency test) to form a swollen transparent gel, the thusly-swollen dressing retaining sufficient fibrous character to be removed as a coherent dressing from a wound. The degree of substitution (D.S.) of the CMC

- 2 -

filaments is preferably at least 0.15, more preferably from 0.2 to 0.5, although it may be up to for example 1.0. The CMC filaments may generally be prepared by reacting cellulose filaments in the presence of strong alkali with 5 chloracetic acid or a salt thereof. The cellulose filaments may be viscose rayon, cuprammonium rayon or cotton, but they are preferably solvent-spun and may accordingly be lyocell.

WO-A-95/19795 discloses a wound dressing which comprises a blend of textile fibres and gel-forming fibres. 10 The textile fibres may be natural or synthetic but are preferably cellulosic fibres such as viscose rayon or cotton. The gel-forming fibres may for example be carboxymethylcellulose or alginate fibres. The gel-forming fibres can be of the type which retain their structural 15 integrity on absorption of exudate or can be of the type which lose their fibrous form and become a structureless gel or a solution on absorption of exudate. The absorbency of the gel-forming fibre (measured by the free-swell method) is desirably at least 2 g/g of 0.9% saline solution, preferably 20 at least 15 g/g, more preferably between 25 and 50 g/g. The D.S. of a carboxymethylcellulose fibre is desirably at least 0.05, preferably at least 0.2, more preferably between 0.3 and 0.5. Such dressings are said to have the advantage that the fibres they contain are not engulfed by new tissue 25 formed during the healing process, so that they can be removed without causing wound injury.

Disclosure of the invention

According to a first aspect of the invention, there is provided a process for the manufacture of a wound dressing 30 comprising the step of carboxymethylating a cellulosic fabric such that the absorbency (as defined hereinafter) of the fabric after carboxymethylation is no more than 3 g/g, preferably no more than 2.5 g/g, further preferably no more than 2 g/g or 1 g/g, greater than the absorbency (as defined 35 hereinafter) of the fabric before carboxymethylation and such that the degree of substitution of cellulose by

- 3 -

carboxymethyl groups in the carboxymethylated fabric measured by IR spectroscopy (as defined hereinafter) is in the range from 0.12 to 0.35, preferably from 0.2 to 0.3. The invention also includes wound dressings which comprise 5 such carboxymethylated fabric.

By the absorbency of the fabric, before and after treatment, we mean the absorbency figures assessed by the method described in British Pharmacopoeia 1993, Addendum 10 1995, page 1706 for Alginate Dressings, but with substitution of the fabric under test for the alginate specified therein, which method yields absorbency in terms of weight per unit area, and then converted to absorbency in terms of weight ratio (g/g) --

15 The cellulosic fabric preferably consists solely of cellulosic fibre but may contain a proportion of non-cellulosic textile fibre or of gel-forming fibre. The cellulosic fibre is of known kind and may be a natural fibre such as cotton or a manmade fibre such as lyocell or viscose 20 rayon; blends of such fibres may be used. We have observed that dressings according to the invention made from cellulosic fibres of low wet strength such as viscose rayon may tend to shed fragments when wetted, and accordingly use of such fibres is generally less preferred. The cellulosic 25 fabric may comprise continuous filament yarn and/or staple fibre. A fabric of continuous filament yarn may be preferred, on the ground that such fabrics are less liable to shed fibre fragments on handling or on removal from a wound. We have nevertheless surprisingly found that 30 dressings according to the invention composed of staple fibres have a low tendency to shed fragments.

The cellulosic fabric is of known kind and may be made in known manner. The basis weight of the fabric is generally in the range from 30 to 250 g/m². The cellulosic fabric may 35 be a woven or knitted fabric or a nonwoven fabric such as a hydroentangled fabric or a needlefelt. A nonwoven fabric

- 4 -

should be of sufficiently robust construction - for example, having sufficiently high fibre entanglement - that the carboxymethylated fabric after absorption of aqueous liquors possesses sufficient mechanical integrity to permit it to be removed from a wound in a single piece.

The carboxymethylation step is generally performed by contacting the fabric with strong alkali, for example sodium hydroxide, and a carboxymethylating agent such as chloracetic acid or a salt thereof such as the sodium salt. These reagents may be applied to the fabric separately or together. The reaction is conveniently performed in an aqueous system. This system preferably comprises a water-miscible organic solvent such as ethanol or industrial methylated spirit, in order to suppress swelling and dissolution of carboxymethylated cellulose. Reference may be made to WO-A-94/16746 for general discussion of the carboxymethylation reaction.

A preferred method of performing such a carboxymethylation step is as follows, and such a method of carboxymethylating a fibre of cellulose II forms a second aspect of the invention. Regenerated or reconstituted cellulose fibre (cellulose II) is contacted with a solution containing from 4 to 8 percent by weight sodium hydroxide, the amount of sodium chloracetate necessary to achieve the desired degree of substitution, from 50 to 60 percent by weight water, and the balance ethanol. For calculation purposes, the solution is considered to consist of the substances applied to the fibre and any moisture introduced with the fibre and/or ethanol. The solution may contain a small proportion of methanol if industrial methylated spirit is used as the source of ethanol. We have found that the presence of lower proportions of water than the specified minimum tends to result in uniform carboxymethylation, which is undesirable in the manufacture of dressings according to the invention. We have found that the presence of greater proportions of water than the specified maximum tends to

- 5 -

result in too low a degree of reaction and too low a degree of slipperiness of the carboxymethylated fibre when wetted. We have further found that lesser proportions of water than those specified above are generally required for
5 satisfactory results on fibres of cellulose I such as cotton. The method is preferably performed at from 40 to 80°C, more preferably from 50 to 60°C. The method is preferably performed for from 20 to 90 min., more preferably from 30 to 60 min. Ethanol may be substituted by another
10 alcohol of the C₁-C₄ group. It will be appreciated that in general the more hydrophobic the alcohol, the lower the proportion of water that is desirable in the solution. Suitable proportions for alcohols other than ethanol can readily be determined by experiment. The method of the
15 second aspect of the invention may be performed on loose fibre, yarn or fabric.

As explained hereinafter, it is thought that the large majority of the carboxymethyl groups in the carboxymethylated material according to the invention is
20 located in the amorphous regions and that only a small minority is located in the crystalline regions. It is thought that the crystalline regions act as entanglement points in the polymeric structure, thus advantageously providing a fabric with good wet strength and also
25 suppressing dissolution of carboxymethylcellulose. It is also thought that the relatively low absorbency is in part a consequence of this phenomenon; but it is one which does not detract from performance in the intended use. It will therefore be understood that severe carboxymethylation
30 conditions, in particular the use of alkali at such a strength or temperature or for such a time that it converts the crystalline regions of cellulose to alkali cellulose thereby enabling reaction in the crystalline regions, are to be avoided.

35 According to a third aspect of the invention, there is provided a carboxymethylated cellulose article wherein the

- 6 -

degree of substitution of cellulose groups measured by IR spectroscopy (as defined hereinafter) is in the range from 0.12 to 0.35, preferably from 0.15 to 0.3 or from 0.2 to 0.3, and wherein the degree of crystallinity measured by NMR 5 (as defined hereinafter) is in the range from 10 to 70 percent, preferably from 15 to 60 or from 20 to 65 percent, more preferably from 30 to 55 percent. The article may take the form of a film, including a perforated film, a foam or sponge, or preferably a fibre. The invention also includes 10 fabrics and dressings which comprise such articles. Wound dressings which comprise fibre according to the third aspect of the invention may conveniently be made by the process and method of the first and second aspects of the invention.

The ^{13}C NMR spectrum of cellulose contains features in 15 the 80-90 ppm region attributable to crystalline cellulose I and/or II. These features are essentially absent from the spectrum of fully carboxymethylated cellulose, such as that disclosed in WO-A-93/12275 and in WO-A-94/16746, and such material is accordingly thought to be amorphous. In 20 contrast, spectra of carboxymethylated cellulose according to the third aspect of the invention exhibit these features to a significant extent, although generally at a somewhat lesser level than do spectra of cellulose I or II. This observation is consistent with the theory that the 25 carboxymethyl groups are mainly located in amorphous rather than crystalline regions.

According to a fourth aspect of the invention, there is provided a method of carboxymethylating an article of cellulose II, wherein the article is contacted with a 30 solution containing sodium hydroxide, sodium chloracetate, ethanol and water, characterised in that the weight ratio of sodium hydroxide to water is in the range from 0.095 to 0.115, preferably from 0.10 to 0.11, and in that the weight ratio of cellulose to water is in the range from 0.22 to 35 0.28, preferably from 0.24 to 0.26. The method is preferably performed at from 40 to 80°C, more preferably from 50 to

- 7 -

60°C. The method is preferably performed for from 20 to 90 min., more preferably from 30 to 60 min. It is thought that the sodium hydroxide concentration may correspond to a swelling maximum for cellulose. The article may be for example a fibre, an article containing a fibre such as a woven, knitted or nonwoven fabric, a film or a sponge. The amount of sodium chloracetate is chosen so as to achieve the desired degree of substitution. The amount of ethanol is chosen so as to achieve a suitable liquor-to-goods ratio. It will be appreciated that a high liquor-to-goods ratio is desirable for voluminous articles such as sponges and bulky nonwovens. Articles made by the method of the fourth aspect of the invention are useful in the manufacture of wound dressings, and the invention includes such dressings. The method of the fourth aspect of the invention can be used to make articles according to the third aspect of the invention.

A carboxymethylated fibre according to the third aspect of the invention made from lyocell or a carboxymethylated fibre made by the methods of the first, second or fourth aspects of the invention from lyocell may have an absorbency of at least 8 g/g of 0.9% (by weight) saline solution, as measured by the free swell method of WO-A-93/12275, and a tenacity of at least 10 cN/tex.

Upon wetting, a fabric dressing according to the invention retains its textile character, swells to a moderate degree and exhibits a desirable surface slipperiness or "gel feel". We have surprisingly found in some cases that such a fabric dressing according to the invention may exhibit a lower absorbency than that of the cellulosic fabric, but that nevertheless when wetted it may exhibit a desirable degree of slipperiness (lubricity) when rubbed between the fingers. By way of guidance, a desirable degree of slipperiness in the present context is somewhat comparable to that observed when fingers wetted with weak soap solution or with dilute aqueous alkali (e.g. 0.01-0.1M

- 8 -

NaOH) are rubbed together. A dressing according to the invention which consists solely of carboxymethylated cellulose fibres has the advantage that it presents a homogeneous surface to the wound.

5 The dressings according to the invention may include or be used in conjunction with a secondary or backing layer of known type, for example an absorbent layer or a layer designed to maintain the wound environment, for example by keeping the wound moist. A backing layer may be affixed
10 before or after the carboxymethylation step. Advantageously, the dressings of the invention may comprise a backing layer of a fusible thermoplastic fibre such as polypropylene, to permit thermal bonding to a further backing layer. Such a fusible backing layer may be incorporated in a fabric
15 dressing by processes known in the manufacture of nonwoven fabrics such as needle bonding, stitchbonding and preferably hydroentanglement. The dressings according to the invention may be medicated. The dressings of the invention may comprise two or more plies of the fabric of the invention.

20 The dressings according to the invention find use particularly as coverings for exuding wounds, more particularly for chronic wounds.

IR Spectroscopy

The degree of substitution of cellulose by
25 carboxymethyl groups (D.S.) was measured by IR spectroscopy as follows. IR spectra were recorded of viscose rayon (D.S. zero), of commercial samples of CMC of known D.S. (0.3, 0.6, 0.85 and 1.05), of a fabric made according to WO-A-94/16746 (D.S. 0.4), and of fabrics in accordance with the
30 invention. Analysis of the spectra of the samples of known D.S. yielded the linear equation:

$$\text{D.S.} = 0.678 * I + 0.05$$

- 9 -

where I is the ratio of the integrated peak intensity over the range 1600-1700 cm^{-1} (C=O stretch) to the integrated peak intensity over the range 1200-1000 cm^{-1} (C-O stretch). By D.S. in relation to the invention we mean the figure 5 estimated using this equation.

The surface and bulk IR spectra of fabrics according to the invention were very similar. This suggests that carboxymethylation had taken place throughout the whole fibre rather than only in the surface regions.

10 The spectra of the fabric according to WO-A-94/16746 and of fabrics of the invention exhibited differences in detail: in particular, the shapes of the broad peak in the O-H stretch region (3500-3000 cm^{-1}) differed, and the C-O stretch region (1200-1000 cm^{-1}) of the fabric of the
15 invention exhibited additional features. These differences could be seen most clearly from second-derivative spectra. The fabrics of the invention derived from rayon and lyocell exhibited sharp peaks at 3445 and 3480 cm^{-1} , attributable to crystalline cellulose II, whereas the sample according to
20 WO-A-94/16746 did not.

NMR Spectroscopy

The degree of crystallinity of carboxymethylated cellulose was measured by NMR spectroscopy as follows. Solid state ^{13}C NMR spectra were obtained at 75 MHz using a Bruker
25 AC3000 (Trade Mark) spectrometer. Measurements were performed on samples packed into 7 mm zirconia rotors using proton-to-carbon cross-polarisation and magic angle spinning (CPMAS). Conditions employed were a magic angle spinning speed of 5.0-5.5 kHz and a 90° proton preparation pulse
30 followed by 2 ms contact time with a pulse recycle time of 3 s. Typically, a thousand scans were acquired on each sample; this is a preferred minimum number. Intensity over the range 50 to 120 ppm was integrated, with background correction. Percentage crystallinity was calculated using

- 10 -

the formula $100(S-R)/S$, where S is the integrated intensity of the sample under test and R is the integrated intensity of a reference sample of CMC prepared according to Example 1 of WO-A-94/16746.

- 5 Without wishing to be bound by theory, the results on articles according to the invention are consistent with substantially uniform carboxymethylation in the amorphous regions but little or no carboxymethylation in the crystalline regions. In contrast, the results on the fabric
10 of WO-A-94/16746 are consistent with substantially uniform carboxymethylation of the whole fibre.

The invention is illustrated by the following Examples, in which parts and proportions are by weight unless otherwise specified:--

15

Example 1

The following cellulosic fabrics were tested:

- A. Continuous filament viscose rayon, warp-knit (Tricotex, Trade Mark of Smith & Nephew), 150 g/m²,
- B. Spun cotton yarn, woven gauze, 227 g/m²,
- 20 C. Lyocell staple fibre, apertured hydroentangled fabric, 60 g/m²,
- D. Lyocell spun yarn, warp-knit, 50 g/m²,
- E. Continuous filament lyocell, weft-knit, ca. 100 g/m²,
- F. Continuous filament lyocell, warp-knit, 40 g/m²,
- 25 G. Continuous filament lyocell, warp-knit, 44 g/m² (tighter fabric construction than F),
- H. Continuous filament lyocell, warp-knit, 68 g/m².

Lyocell staple fibre was supplied by Courtaulds plc under the Trade Mark COURTAULDS LYOCCELL and is now available
30 from the same entity under its new name Akzo Nobel UK Limited. Continuous filament lyocell was supplied by Akzo Nobel AG under the Trade Mark NEWCELL.

- 11 -

These cellulosic fabrics were carboxymethylated using the following general method. Sodium hydroxide and sodium chloracetate are separately dissolved in equal volumes of water. The two solutions are added to a reaction vessel
5 together with a weighed quantity of industrial methylated spirit (IMS) and the mixture is stirred to yield a homogeneous solution. A sample of fabric is immersed in the solution and the vessel is sealed. The vessel is then stored with occasional agitation in a preheated waterbath for the
10 required time. The fabric is next removed from the vessel and squeezed by hand to remove excess liquor. Glacial acetic acid is added to the vessel to make the solution acidic, and the fabric is replaced in the solution. The vessel is then replaced in the waterbath for ten minutes with agitation.
15 The liquor is then discarded. The fabric is placed in a crystallising dish and a first wash liquor is added; the fabric and liquor are then transferred into the reaction vessel in the waterbath for washing with hot wash liquor. The fabric is treated in similar manner with a second wash
20 liquor and with a final wash liquor containing soft finish, after which it is set aside to dry at room temperature. Detailed conditions for the two methods referred to hereinafter as Methods I and II are given in Table 1:

- 12 -

Table 1

	Method I	Method II
Reaction		
Fabric weight g (air-dry)	50	50
5 Fabric moisture content %	10	10
Temperature °C	70	60
Sodium hydroxide g	19.1	19.1
Sodium chloracetate g	28.7	28.7
Water g (including fibre moisture)	117.5	175
10 IMS g	167.5	110
NaOH/water g/g	0.163	0.109
Cellulose/water g/g	0.383	0.257
Neutralisation		
Acetic acid ml	35	35
15 First Wash Liquor		
Water ml	118	118
IMS ml	192.5	192.5
Citric acid g	1.6	1.6
Second Wash Liquor		
20 Water ml	118	118
IMS ml	192.5	192.5
Soft Finish Wash Liquor		
Water ml	29	29
IMS ml	307.5	307.5
25 Tween finish g	1.7	1.7
(TWEEN is a Trade Mark of ICI Americas, Inc.)		

The method referred to below as II* is method II, but with the temperature in the reaction step being 70°C.

The carboxymethylated fabrics were wetted with saline
 30 solution, and their slipperiness or "gel feel" was assessed manually and ranked on an arbitrary numerical scale, in which higher values represent greater slipperiness and a value in the range of around 4 to 10, preferably 5, represents a subjectively desirable degree of slipperiness
 35 for a wetted non-adherent dressing based on experience. The results shown in Table 2 were obtained:

- 13 -

Table 2

Fabric	A	B	B	C	D	D	E	E	F	G	H
Method	II	I	II	II	I	II	I	II	II*	II*	II*
Time min											
5 0	0	0	0	0	0	0	0	0	-	-	-
15	2	5	0	4	-	2	-	1	-	-	-
30	5	5	0	6	-	5	-	1	-	-	-
45	7	5	1	5	12	7	15	4	-	-	-
60	9	6	2	8	-	9	-	8	-	-	-
10 70	-	-	-	-	-	-	-	-	5	5	5
75	10	6	3	6	-	-	-	6	-	-	-
90	13	6	3	6	-	-	-	6	-	-	-

A dash in this and subsequent Tables indicates that no measurement was made.

- 15 The absorbency of the fabrics was measured, and the results shown in Table 3 were obtained:

Table 3

Fabric	A	B	C	D	F	G	H
Method	II	I	II	II	II*	II*	II*
20 Time min							
0 (control)	2.5	8.0	9.4	6.2	2.6	2.9	2.6
15	-	7.6	9.7	-	-	-	-
30	-	7.0	10.1	5.0	-	-	-
45	2.4	6.5	9.6	-	-	-	-
25 60	-	7.5	10.2	-	-	-	-
70	-	-	-	-	4.4	5.0	4.8
75	-	-	10.3	-	-	-	-
90	-	-	12.3	-	-	-	-

D.S. measurements on treated fabrics are recorded in
30 Table 4:

- 14 -

Table 4

Fabric	A	B	C	D	F	G	H
Method	II	I	II	II	II*	II*	II*
Time min							
5 15	0.17	0.14	0.17	0.18	-	-	-
30	0.22	0.18	0.16	0.21	-	-	-
45	0.22	0.14	0.20	0.23	-	-	-
60	0.31	0.20	0.26	-	-	-	-
70	-	-	-	-	0.21	0.24	0.20
10 75	0.38	0.25	0.20	-	-	-	-
90	0.35	0.30	0.21	-	-	-	-

The relationship between D.S. and gel feel is thus broadly linear.

Example 2

- 15 Samples of lyocell tow were carboxymethylated according to Method II of Example 1, with the differences and further details indicated in Table 5, which also reports experimental results:

Table 5

20 Reaction	Reaction	Water in	NaOH/	Cellulose/	FSA Gel feel
temp.	time min	solution	water	water	g/g
°C	min	wt. %	g/g	g/g	
-	-	-	-	-	17.8 0
70	65	36.8	0.154	0.362	36.4 15
25 70	65	47.0	0.120	0.283	29.0 12
70	65	51.8	0.109	0.257	21.0 9
70	65	53.6	0.106	0.248	18.0 10
60	65	53.6	0.106	0.248	16.4 5
60	30	53.6	0.106	0.248	17.3 5
30 60	65	61.7	0.092	0.216	17.4 3
60	65	68.3	0.083	0.195	11.4 2

- 15 -

The first entry in Table 5 represents an untreated control. Free-swell absorbency (FSA) was measured according to WO-A-94/16746. Solution weight was maintained constant throughout this series of experiments.

5

Example 3

The degree of crystallinity of samples of carboxymethylated cellulose was measured by ^{13}C NMR. The results shown in Table 6 were obtained:

Table 6

10 Sample	Method	Time min	Crystallinity %
A	II	75	24
B	I	30	53
B	I	75	48
B	II	60	63
15 C	II	50	42
C	II	60	37
CMC	-	-	0

These measurements were made on the samples described in Example 1, except that (1) the "C" samples were additional to Example 1, and (2) the CMC sample was a carboxymethylated fibre prepared according to the teachings of WO-A-94/16746, as described more fully below. It can be seen by comparing Tables 2 and 6 that decreasing crystallinity generally corresponds with increasing gel feel.

The CMC sample was prepared as follows. Air-dry lyocell fibre, an aqueous solution of sodium hydroxide, ethanol, and an aqueous solution of sodium chloracetate were charged into a reactor to yield a mixture containing bone-dry cellulose (9 kg), sodium hydroxide (3.8 kg), sodium monochloracetate (5.7 kg), water (24.3 kg, including water introduced with the fibre) and ethanol (26.1 kg). Thus, the NaOH/water ratio

- 16 -

was 0.156 and the cellulose/water ratio was 0.370. The reactor was heated at 70°C for 65 min. Acetic acid (7 l) was added to the mixture and the temperature was maintained at 70°C for 10 min. Excess liquor was removed by blowing down 5 with nitrogen. The fibre was washed with a solution of citric acid (0.3 kg) in water (23 kg) and ethanol (30 kg) at 70°C for 10 min. Excess liquor was removed by blowing down with nitrogen. The washing and blowing-down stages were repeated. The fibre was then washed with a solution of soft 10 finish (0.3 kg) in water (6 kg) and ethanol (48 kg) at 70°C for 10 min. Excess liquor was removed by blowing down with nitrogen, and the CMC fibre was dried in an air dryer.

Example 4

A laminate was made by laying-up a web of lyocell 15 staple fibre (33 g/m²) and a nonwoven polypropylene backing scrim (7.5 g/m²) followed by hydroentangling (6 heads: pressure 2x40 and 4x60 bar) from the lyocell side. The lyocell fibre in the resulting laminate was carboxymethylated by method II of Example 1. The 20 polypropylene side of the carboxymethylated laminate was readily adhered to a nonwoven fabric backing of viscose staple fibre (330 g/m²) by application of heat using a domestic iron.

Similar results were obtained using a web of lyocell 25 staple fibre (48 g/m²) and a polypropylene scrim (12 g/m²) hydroentangled together (8 heads; pressure 2x40, 4x60 and 2x80 bar).

Example 5

Cellulose sponge (25 g; in the form of a sheet roughly 5 mm 30 thick, as used for domestic cleaning purposes; bulk density 0.08 g/ml) was placed in a 1000 ml flask. To the flask was added a solution of 9.55 g sodium hydroxide in 40 g water and a solution of 14.35 g sodium chloracetate in a mixture

- 17 -

of 44 g. water and 270 g IMS. The total amount of water (including that originating from the sponge) was 89.2 g. Thus, the NaOH/water ratio was 0.107 and the cellulose/water ratio was 0.252. The flask was heated at 70°C for 1 hr. To 5 the flask was added 17.5 ml glacial acetic acid. The flask was allowed to stand for 5-10 min. The liquor was discarded, and the sponge was washed with a solution of 0.8 g citric acid in a mixture of 84 ml water and 137 ml IMS. The wash liquor was discarded and the washing step repeated. The wash 10 liquor was again discarded and the sponge washed with a mixture of 0.85 g Tween finish, 25 ml water and 265 ml IMS. The liquor was discarded and the sponge washed with a mixture of 30 g glycerol, 30 ml water and 40 ml IMS. The liquor was discarded and the sponge dried at ambient 15 temperature. The glycerol served as softening agent to prevent the sponge becoming hard and board-like on drying. These reaction conditions differ from those of Example 1 essentially in the use of greater liquid volumes to cater for the low bulk density of the sponge. Reaction volumes may 20 be reduced if a compressed sponge is used. The "gel feel" of the sponge before and after carboxymethylation was 0 and 5 respectively. The D.S. of the carboxymethylated sponge was 0.30 and the crystallinity 30%.

Example 6

25 A sample of fabric A of Example 1 (50 g air-dry) was carboxymethylated according to the general procedure of Example 1. The treatment solution contained 19.1 g NaOH, 28.7 g sodium chloracetate, 121.2 g IMS and 171.0 g water (including moisture from the fabric). Thus, the NaOH/water 30 ratio was 0.112 and the cellulose/water ratio was 0.263. The reaction was conducted for 40 min at 70°C. The "gel feel" of the resulting product was 5, the D.S. 0.15 and the crystallinity 17%.

- 18 -

Example 7

A roll of fabric A of Example 1 (1250 g air-dry; 10% moisture; 17 cm diameter x 22 cm long) was carboxymethylated in a kier according to the general procedure of Example 1. The treatment solution contained 478.1 g NaOH, 717.2 g sodium chloracetate, 4241.8 g IMS and 4275 g water (including moisture from the fabric). Thus, the NaOH/water ratio was 0.112 and the cellulose/water ratio was 0.263. The reaction was conducted for 40 min at 70°C. The "gel feel" of the resulting product was 6, the D.S. 0.23 and the crystallinity 24%.

Example 8

A sample of a bulky apertured nonwoven fabric of lyocell fibre (50 g air-dry; 10% moisture; basis weight 65 g/m²) was carboxymethylated according to the general procedure of Example 1. The treatment solution contained 19.1 g NaOH, 28.7 g sodium chloracetate, 231.2 g IMS and 171.0 g water (including moisture from the fabric). Thus, the NaOH/water ratio was 0.112 and the cellulose/water ratio was 0.263. The reaction was conducted for 30 min at 65°C. The "gel feel" of the resulting product was 5, the D.S. 0.31 and the crystallinity 26%.

Example 9

A roll of the fabric used in Example 8 (4.50 kg air-dry; 39 cm diameter x 28 cm long) was carboxymethylated in a kier according to the general procedure of Example 1. The treatment solution contained 1.72 kg NaOH, 2.58 kg sodium chloracetate, 44.89 kg IMS and 15.77 kg water (including moisture from the fabric). Thus, the NaOH/water ratio was 0.109 and the cellulose/water ratio was 0.257. The reaction was conducted for 30 min at 60°C. The "gel feel" of the resulting product was 4, the D.S. at the outside and inside of the roll was 0.18 and 0.17 respectively and the

- 19 -

crystallinity at the outside and inside of the roll was 28% and 31% respectively.

Example 10

A roll of cotton gauze (23 g/m²; 7.50 kg air-dry, 6.75 kg
5 bone-dry) (cellulose I) was carboxymethylated in a kier
according to the general procedure of Example 1. The
treatment solution contained 2.87 kg NaOH, 4.30 kg sodium
chloracetate, 19.60 kg IMS and 18.23 kg water (including
moisture from the fabric). Thus, the NaOH/water ratio was
10 0.157 and the cellulose/water ratio was 0.370. The reaction
was conducted for 65 min at 70°C. The "gel feel" of the
resulting product was 6, the D.S. ranged from 0.16 to 0.21,
and the crystallinity was 42%.

- 20 -

CLAIMS

1. A process for the manufacture of a wound dressing comprising the step of carboxymethylating a cellulosic fabric such that the absorbency (as defined) of the fabric after carboxymethylation is no more than 3 g/g greater than the absorbency (as defined) of the fabric before carboxymethylation and such that the degree of substitution of cellulose by carboxymethyl groups in the carboxymethylated fabric measured by IR spectroscopy (as defined) is in the range from 0.12 to 0.35.
2. A process according to claim 1, characterised in that the absorbency (as defined) of the fabric after carboxymethylation is no more than 2.5 g/g greater than the absorbency (as defined) of the fabric before carboxymethylation.
3. A process according to claim 1, characterised in that the absorbency (as defined) of the fabric after carboxymethylation is no more than 1 g/g greater than the absorbency (as defined) of the fabric before carboxymethylation.
4. A process according to any one of the preceding claims, characterised in that the degree of substitution of cellulose by carboxymethyl groups in the carboxymethylated fabric measured by IR spectroscopy (as defined) is in the range from 0.2 to 0.3.
5. A process according to any one of the preceding claims, characterised in that the fabric comprises cellulosic continuous filament yarn.
6. A process according to any one of the preceding claims, characterised in that the fabric comprises lyocell fibre.
7. A method of carboxymethylating a fibre of cellulose II, wherein the fibre is contacted with a solution containing

- 21 -

from 4 to 8 percent by weight sodium hydroxide, sodium chloracetate, from 50 to 60 percent by weight water, and the balance ethanol, such that the degree of substitution of cellulose by carboxymethyl groups in the carboxymethylated 5 fibre measured by IR spectroscopy (as defined) is in the range from 0.12 to 0.35.

8. A method according to claim 7, wherein the degree of substitution of cellulose by carboxymethyl groups in the carboxymethylated fibre measured by IR spectroscopy (as 10 defined) is in the range from 0.2 to 0.3.

9. A carboxymethylated cellulose article wherein the degree of substitution of cellulose groups measured by IR spectroscopy (as defined) is in the range from 0.12 to 0.35 and wherein the degree of crystallinity measured by NMR (as 15 defined) is in the range from 10 to 70 percent.

10. A carboxymethylated article according to claim 9, characterised in that the degree of substitution measured by IR spectroscopy (as defined) is in the range from 0.2 to 0.3.

20 11. A carboxymethylated article according to one of claim 9 and claim 10, characterised in that the degree of crystallinity measured by NMR (as defined) is in the range from 15 to 60 percent.

12. A carboxymethylated article according to any one of 25 claims 9 to 11, characterised in that it is the form of a fibre or of a fabric comprising such fibre.

13. A carboxymethylated article according to any one of claims 9 to 12, characterised in that it is made from lyocell and has an absorbency of at least 8 g/g of 0.9% (by 30 weight) saline solution as measured by the free swell method of WO-A-93/12275, and a tenacity of at least 10 cN/tex.

- 22 -

14. A carboxymethylated article according to any one of claims 9 to 11 or 13, characterised in that it is the form of a foam or sponge.

15. A method of carboxymethylating an article of cellulose
5 II wherein the article is contacted with a solution containing sodium hydroxide, sodium chloracetate, ethanol and water, characterised in that the weight ratio of sodium hydroxide to water is in the range from 0.095 to 0.115, and in that the weight ratio of cellulose to water is in the
10 range from 0.22 to 0.28.

16. A method according to claim 15, characterised in that the weight ratio of sodium hydroxide to water is in the range from 0.10 to 0.11.

17. A method according to one of claims 15 and 16,
15 characterised in that the weight ratio of cellulose to water is in the range from 0.24 to 0.26.

18. A method according to any one of claims 15 to 17, characterised in that the article is a fibre.

19. A method according to any one of claims 15 to 17,
20 characterised in that the article is a sponge.

20. A wound dressing made by the process of any one of claims 1 to 6 or comprising fibre made by the method of one of claim 7 and claim 8 or comprising an article according to any one of claims 9 to 14 or comprising an article made by
25 the method of any one of claims 15 to 19.

21. A wound dressing according to claim 20, characterised in that it includes a backing layer.

22. A wound dressing according to claim 21, characterised in that the backing layer comprises a fusible thermoplastic
30 fibre.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/02093

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61L15/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L C08B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 579 943 A (KAMIDE KENJI ET AL) 1 April 1986 (1986-04-01) column 4, line 1 - line 45 examples tables ----	1-22
X	WO 93 12275 A (COURTAULDS PLC) 24 June 1993 (1993-06-24) abstract page 3, line 2 - page 5, line 23 examples 1,4,5,15,20 ----	1-6,9-14
X	US 4 405 324 A (CRUZ JR MAMERTO M) 20 September 1983 (1983-09-20) table 4 examples 1-3 ----- -/--	1-6

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"G" document member of the same patent family

Date of the actual completion of the international search

15 October 1999

Date of mailing of the international search report

22/10/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 551 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Muñoz, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/02093

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 256 877 A (KARLSSON ALF H ET AL) 17 March 1981 (1981-03-17) column 1, line 16 - line 45 -----	1-6

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/02093

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-8 and 20-22 relate to a method defined by reference to a desirable characteristic or property, namely the absorbency of the final product compared to that of the untreated product and the degree of substitution obtained through carboxymethylation of a cellulosic product.

The claims cover all methods/products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the method by reference to a result to be achieved.

Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the method as defined in examples 1-10 and taking in consideration the desired characteristics of the final product namely absorbency properties and degree of carboxymethylation.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/02093

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4579943 A	01-04-1986	JP 1044201 B JP 60094401 A	26-09-1989 27-05-1985
WO 9312275 A	24-06-1993	AT 172254 T AU 667068 B AU 3164293 A BR 9206900 A CA 2125291 A CZ 9401357 A DE 69227318 D DE 69227318 T EP 0616650 A ES 2125323 T FI 942716 A JP 7502081 T NO 942144 A NZ 246174 A SK 69194 A US 5731083 A	15-10-1998 07-03-1996 19-07-1993 21-11-1995 24-06-1993 15-12-1994 19-11-1998 12-05-1999 28-09-1994 01-03-1999 09-06-1994 02-03-1995 09-06-1994 26-10-1995 09-11-1994 24-03-1998
US 4405324 A	20-09-1983	NONE	
US 4256877 A	17-03-1981	SE 430609 B AT 367298 B AT 908177 A AU 504848 B AU 3172977 A BE 862130 A CA 1108364 A CH 634234 A DE 2757096 A DK 568477 A FI 773861 A, B, FR 2375362 A GB 1570040 A IE 46213 B IT 1093078 B JP 1152846 C JP 53084050 A JP 57045179 B LU 78741 A NL 7714216 A SE 7614342 A YU 302577 A	28-11-1983 25-06-1982 15-11-1981 01-11-1979 28-06-1979 21-06-1978 08-09-1981 31-01-1983 22-06-1978 22-06-1978 22-06-1978 21-07-1978 25-06-1980 06-04-1983 19-07-1985 30-06-1983 25-07-1978 27-09-1982 11-07-1978 23-06-1978 22-06-1978 21-01-1983

Form PCT/ISA/210 (patent family annex) (July 1992)

THIS PAGE BLANK (USPTO)